More compelling evidence on why earlier HIV treatment lengthens survival

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A study showing improved survival of starting antiretroviral treatment earlier than current U.S. recommendations is being reported in the April 30 issue of the *New England Journal of Medicine*. The study found that not starting HIV patients at a CD4 count greater than 500 cells per cubic millimeter increased risk of death by 94 percent.

"The question of when to start antiretroviral therapy has been one of the key controversies in HIV care for over a decade" said University of Washington's Dr. Mari Kitahata, the lead researcher on the study. "Our study adds a lot of weight to the growing body of evidence that starting treatment earlier in HIV disease prolongs survival."

Current U.S. guidelines recommend treatment for asymptomatic patients who have a CD4 count of less than 350. However, these guidelines lack data from randomized clinical trials regarding the timing of antiretroviral therapy.

Since 1996, when potent antiretroviral therapy was introduced and recommended for asymptomatic HIV patients with a CD4 count less than 500 cells per cubic millimeter, there has been uncertainty about when to start treatment.

The article, "Effect of Early versus Deferred Antiretroviral Therapy for HIV on Survival," reports on two analyses of 17,517 asymptomatic patients with HIV infection receiving care between 1996 and 2006. The data were gathered through a recent collaboration of 22 research groups in more than 60 sites in the United States and Canada -- the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD).

In order to study the impact of earlier initiation of therapy, researchers needed a large number of patients at high CD4+ counts who are observed for a long period of time to a definitive endpoint of death. Because of the combined effort of one of the largest collaborations of HIV cohorts and researchers, researchers had the data to examine the effect of early AIDS treatment.

Results from the first analysis were announced Oct. 2008 at the 48th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy/46th Annual IDSA Meeting Washington DC. Among the 8,632 patients with a CD4+ count+ 351 to 500, those who deferred antiretroviral therapy until the CD4+ count was below 350 had an increase of 69% in the risk of death.

Results from the second analysis were announced Feb 2009 at the 16th Annual Conference on Retroviruses and Opportunistic Infections in Montreal, Canada. Among the 9,155 patients with a CD4+ count above 500, those who deferred antiretroviral therapy until the CD4+ count was below 500 had an increase of 94% in the risk of death.

About 1.1 million people in the United States are infected with HIV, the virus that causes AIDS, according the U.S. Centers for Disease Control and Prevention. Worldwide, about 33 million people are infected with HIV, according to UNAIDS.

In the past, recommendations for when to start antiretroviral therapy shifted to waiting until later in HIV disease to lower CD4+ counts because of concern for resistance and toxicities of treatment. New treatments, however, are more potent, have fewer side effects and have to be taken less frequently, said Kitahata.

Additional benefits of earlier therapy for HIV include greater likelihood of achieving a normal CD4+ count and reduction in inflammation and immune activation that result in potentially irreversible immune-system and end-organ damage, such as cardiovascular, liver and renal disease. Results of the study suggest that the side effects of treatment are less deleterious than untreated HIV infection.

The decision to begin antiretroviral therapy is one each individual makes in consultation with their doctor. Kitahata said that If an asymptomatic individual has a CD4+ count greater than 500 and is ready to begin therapy, it should be started in conjunction with ongoing monitoring for potential side effects that could arise.

More information:

Original Article:
content.nejm.org/cgi/content/full/NEJMoa0807252
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content.nejm.org/cgi/content/full/NEJMe0902713

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